



CASE 4-20918B/N1

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450

Dolores DeCarminie
Type or print nameDolores DeCarminie
Signature5/22/03
Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE ISSUED PATENT 6,465,504 OF

RENE LATTMANN ET AL

ISSUED: OCTOBER 15, 2002

APPLICATION NO.: 09/699,765

FILED: OCTOBER 30, 2000

FOR: SUBSTITUTED 3,5-DIPHENYL-1,2,4-
TRIAZOLES AND THEIR USE AS
PHARMACEUTICAL METAL CHELATORS**Certificate****MAY 29 2003****of Correction**ATTENTION: CERTIFICATE OF CORRECTION BRANCHCommissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450REQUEST FOR CERTIFICATE OF CORRECTION UNDER CFR § 1.322

Sir:

Pursuant to 37 CFR 1.322, it is hereby respectfully requested that a Certificate of Correction be issued for United States Patent 6,465,504 containing the corrections set forth on the appended Form PTO 1050.

On the title page, in item (75), the **Inventors'** information was incorrect. The country where the two inventors reside **should be Switzerland and not Sweden**. Also, in item (30), the "**Foreign Application Priority Data**" listed the country where the application was filed incorrectly. The country is also **Switzerland**. Note that the attached copy of the Declaration clearly shows this to be true.

Each of the other errors is believed to be attributable to the Patent and Trademark Office as is evident as shown in the table on page 2:

<u>Location and/or Error in Printed Patent</u>	<u>Location of Support in *Specification or **Amendment</u>
Column 7, line 63, replacement of "alkoXY" with alkoxy"	*Page 11, line 11 beneath the structural formula
Column 8, line 10, replacement of "I" with "II"	*Page 11, line 18 beneath the structural formula
Column 16, last line, replacement of "1.7 9" with "1.7 g"	*Page 24, third line of Example 18
Column 17, line 17, replacement of "tazole" with "triazole"	*Page 24, fifth line of Example 19
Column 17, line 58, replacement of "268-269- 269° C." with "268-269° C."	Page 25, sixth line of Example 21
Column 18, line 24, replacement of "13,5" with "[3,5"	*Page 26, second line of Example 24
Column 19, line 34, replacement of "ace" with "acetamide"	*Page 27, seventh line of Example 29
Column 19, line 42, replacement of "1.09" with "1.0 g"	*Page 27, third line of Example 30
Column 19, line 53, after "4.9 (s,2H)", insertion of "7.0 (m, 4H)" and replacement of "7.4 (m,3H)" with "7.4 (m, 3H)"	*Page 28, line 3 and 4

Enclosed are copies of pages 11, 24, 25, 26, 27 and 28, which clearly show the location of support.

Attached is a duplicate of Form PTO 1050, with at least one copy being suitable for printing.

Since the above errors are not ascribable to the patentees, no fee is believed to be necessitated by this Request for Certificate of Correction. However, in the event that a fee is required, the Commissioner is hereby authorized to charge said fee to Deposit Account No. 19-0134 in the name of Novartis.

Please send the Certificate of Correction to the address currently associated with Customer No. 001095, viz:

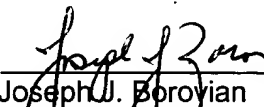
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Respectfully submitted,

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Encls.: Form PTO 1050 (2)
copy of Declaration
copies of pages 11, 24, 25, 26, 27 and 28
postcard

Date: May 22, 2003



Joseph J. Borovian
Agent for Patentees
Reg. No. 26,631

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO : 6,465,504 B1
DATED: : OCTOBER 15, 2002
INVENTOR(S) : RENE LATTMANN ET AL

It is certified that there are errors in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title page

Item (75) should read:

-- (75) Inventors: **René Lattmann**, Binningen; **Pierre Acklin**, Basel, both of (CH) --.

Item (30) should read:

-- (30) **Foreign Application Priority Data**
Jun. 25, 1996 (CH)1593/96 --.

Column 7

Line 63 should read:

-- alkyl, halo-lower alkyl, lower alkoxy or nitrile; R₆ and --.

Column 8

Line 10 should read:

-- formula II in which --.

MAILING ADDRESS OF SENDER:

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PATENT NO. 6,465,504 B1

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO : 6,465,504 B1
DATED: : OCTOBER 15, 2002
INVENTOR(S) : RENE LATTMANN ET AL

It is certified that there are errors in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 16

Last line should read:

-- [1,3]oxazin-4-one are boiled under reflux for 5 h with 1.7 g --.

Column 17

Line 17 should read:

-- dimethylaminobenzyl)-1H-[1,2,4]triazole remains as colorless --.

Line 58 should read:

-- remains as colorless crystals of m.p. 268-269° C. --.

Column 18

Line 24 should read:

--2.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol- --.

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PATENT NO. 6,465,504 B1

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO : 6,465,504 B1
DATED: : OCTOBER 15, 2002
INVENTOR(S) : RENE LATTMANN ET AL

It is certified that there are errors in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 19

Line 34 should read:

-- ethoxy)ethyl]acetamide remains as colorless crystals of m.p --.

Line 42 should read:

-- yl]acetate (Example2) and 1.0 g of N,N-bis(2-hydroxyethyl) --.

Line 53 should read:

-- 2H), 4.9 (s, 2H), 7.0 (m, 4H), 7.4 (m, 3H), 7.95 (d, 1H), 8.1 (t, 1H), 11.0 --.

MAILING ADDRESS OF SENDER:

Joseph J. Borovian

Novartis

Corporate Intellectual Property

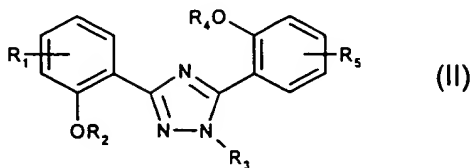
One Health Plaza, Building 430

East Hanover, NJ 07936-1080

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PATENT NO. 6,465,504 B1

The present invention also makes available novel compounds of the general formula II



in which

R_1 and R_5 simultaneously or independently of one another are hydrogen, halogen, lower-alkyl, halo-lower alkyl, lower alkoxy, halo-lower alkoxy, carboxyl, carbamoyl, N-lower alkylcarbamoyl, N,N-di-lower alkylcarbamoyl or nitrile; R_2 and R_4 simultaneously or independently of one another are hydrogen, unsubstituted or substituted lower alkanoyl or aroyl, or a radical which can be removed under physiological conditions, e.g. a protective group; R_3 is $R_6R_7N-C(O)$ -lower alkyl, unsubstituted or substituted aryl, aryl-lower alkyl, substituted by N-lower alkylamino, N,N-di-lower alkylamino or pyrrolidino, or unsubstituted or substituted heteroaryl or heteroaralkyl, with the proviso that R_3 is not phenyl or phenyl substituted by halogen, nitro, nitrile, hydroxyl, lower alkyl, halo-lower alkyl, lower alkoxy or lower alkoxy-carbonyl if R_2 and R_4 are hydrogen, and R_1 and R_5 are hydrogen, halogen, lower alkyl, halo-lower alkyl, lower alkoxy or nitrile; R_6 and R_7 simultaneously or independently of one another are hydrogen, lower alkyl, hydroxy-lower alkyl, alkoxy-lower alkyl, hydroxyalkoxy-lower alkyl, amino-lower alkyl, N-lower alkylamino-lower alkyl, N,N-di-lower alkylamino-lower alkyl, N-(hydroxy-lower alkyl)amino-lower alkyl, N,N-di(hydroxy-lower alkyl)amino-lower alkyl or, together with the nitrogen atom to which they are bonded, form an azaalicyclic ring; and salts thereof.

Primarily, the invention relates to compounds of the formula II, in which

R_1 and R_5 simultaneously or independently of one another are hydrogen, halogen, lower alkyl, halo-lower alkyl, lower alkoxy or halo-lower alkoxy; R_2 and R_4 simultaneously or independently of one another are hydrogen or a radical which can be removed under physiological conditions, e.g. a protective group; R_3 is $R_6R_7N-C(O)$ -lower alkyl, substituted aryl, aryl-lower alkyl, substituted by N-lower alkylamino, N,N-di-lower alkyl amino or pyrrolidino, or unsubstituted or substituted heteroaralkyl with the proviso that R_3 is not phenyl, substituted by halogen, nitro,

is stirred for a further 1 h and the solvent is then distilled off under reduced pressure. The residue is suspended in 200 ml of ethanol, filtered off and washed with ethanol. After drying, 6-chloro-2-(5-chloro-2-hydroxyphenyl)benz[e][1,3]oxazin-4-one is obtained as slightly yellow crystals of m.p. 246-248 C.

Example 17: 4-[3,5-Bis(5-chloro-2-hydroxyphenyl)-[1,2,4]triazol-1-yl]benzoic acid

3.0 g of 6-chloro-2-(5-chloro-2-hydroxyphenyl)benz[e][1,3]oxazin-4-one and 1.7 g of 4-hydrazinobenzoic acid are boiled under reflux for 2 h in 40 ml of ethanol. The crystals precipitating on cooling are recrystallized from isopropanol. After drying, 4-[3,5-bis(5-chloro-2-hydroxyphenyl)-[1,2,4]triazol-1-yl]benzoic acid remains as colorless crystals of m.p. 275-278 C.

Example 18: 3,5-Bis(5-chloro-2-hydroxyphenyl)-1-(pyridin-2-ylmethyl)-1H-[1,2,4]triazole

3.0 g of 6-chloro-2-(5-chloro-2-hydroxyphenyl)benz[e][1,3]oxazin-4-one are boiled under reflux for 5 h with 1.7 g of 2-hydrazinomethylpyridine hydrochloride and 3 ml of triethylamine in 50 ml of ethanol. The crystals precipitating on cooling are washed with ethanol. After drying, 3,5-bis(5-chloro-2-hydroxyphenyl)-1-(pyridin-2-ylmethyl)-1H-[1,2,4]triazole remains as colorless crystals of m.p. 227-229 C.

Example 19: 3,5-Bis(5-chloro-2-hydroxyphenyl)-1-(4-dimethylaminobenzyl)-1H-[1,2,4]triazole

3.0 g of 6-chloro-2-(5-chloro-2-hydroxyphenyl)benz[e][1,3]oxazin-4-one are boiled under reflux for 4 h with 2.2 g of 4-dimethylaminobenzylhydrazine hydrochloride and 3 ml of triethylamine in 50 ml of ethanol. The crystals precipitating on cooling are washed with ethanol. After drying, 3,5-bis(5-chloro-2-hydroxyphenyl)-1-(4-dimethylaminobenzyl)-1H-[1,2,4]triazole remains as colorless crystals of m.p. 205-207 C.

Example 20: 4-[3,5-Bis(5-fluoro-2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-benzoic acid

2.5 g of 6-fluoro-2-(5-fluoro-2-hydroxyphenyl)benz[e][1,3]oxazin-4-one and 1.6 g of 4-hydrazinobenzoic acid are boiled under reflux for 3 h in 25 ml of ethanol. The mixture is cooled, poured onto water and extracted with ethyl acetate. The combined organic phases are dried over sodium sulfate and concentrated on a rotary evaporator. The residue is crystallized from ethyl

acetate/hexane. After drying, 4-[3,5-bis(5-fluoro-2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-benzoic acid remains as colorless crystals of m.p. 252-255 C.

The starting material can be prepared, e.g., as follows:

a) 6-Fluoro-2-(5-fluoro-2-hydroxyphenyl)benz[e][1,3]oxazin-4-one: 4.3 g of 5-fluoro-salicylamide and 4.7 g of 5-fluorosalicylic acid are boiled under reflux in 50 ml of xylene after addition of 0.3 ml of pyridine. 4.4 ml of thionyl chloride are added in the course of 2 h, the mixture is stirred for a further 1 h and the solvent is then distilled off under reduced pressure. The residue is suspended in 30 ml of ethanol, filtered off and washed with ethanol. After drying, 6-fluoro-2-(5-fluoro-2-hydroxyphenyl)benz[e][1,3]oxazin-4-one is obtained as slightly yellow crystals of m.p. 250-252 C.

Example 21: 4-[3,5-Bis(2-hydroxy-5-methylphenyl)-[1,2,4]triazol-1-yl]benzoic acid

1.15 g of 2-(6-hydroxy-*m*-tolyl)-6-methyl-4*H*-[1,3]benzoxazin-4-one in [CAS-Reg.-No.:24798-62-7] and 0.6 g of 4-hydrazinobenzoic acid are boiled under reflux for 2 h in 15 ml of ethanol. The crystals precipitating on cooling are crystallized from isopropanol. After drying, 4-[3,5-bis(2-hydroxy-5-methylphenyl)-[1,2,4]triazol-1-yl]benzoic acid remains as colorless crystals of m.p. 268-269°C.

Example 22: [3,5-Bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetic acid

0.6 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetate (Example 2) is dissolved in 20 ml of methanol with 0.4 g of sodium hydroxide and the mixture is stirred at room temperature for 2 h. It is acidified with 0.1 N hydrochloric acid and the precipitated crystals are filtered off. After washing with water and drying, [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetic acid remains as colorless crystals of m.p. 231-233 °C.

Example 23: 2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-methylacetamide

2.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetate (Example 2) are dissolved in 15 ml of ethanol and treated with 0.8 ml of 8M methylamine in ethanol. The mixture is stirred at 60 °C for 3 h and then cooled. The crystals precipitating in the course of this are filtered off and

washed with ethanol. After drying, 2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-methylacetamide remains as colorless crystals m.p. 247-249 °C.

Example 24: 2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-(2-hydroxyethyl)acetamide

2.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetate (Example 2) are dissolved in 10 ml of ethanolamine and stirred at room temperature for 2 h. The mixture is concentrated to dryness in vacuo and the residue is crystallized from isopropanol. After drying, 2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-(2-hydroxyethyl)acetamide remains as colorless crystals of m.p. 208-211 °C.

Example 25: 2-[3,5-Bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-(2-methoxyethyl)acetamide

4.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetate (Example 2) are dissolved in 30 ml of 2-methoxyethylamine and the mixture is stirred at room temperature for 2 h. It is concentrated to dryness in vacuo and the residue is crystallized from isopropanol. After drying, 2-[3,5-Bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-(2-methoxyethyl)acetamide remains as colorless crystals of m.p. 184-186 °C.

Example 26: 2-[3,5-Bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-(2,3-dihydroxypropyl)-acetamide

2.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetate (Example 2) and 2.4 g of (+/-)3-amino-1,2-propanediol are heated at 60°C for 2 h in 10 ml of ethanol. The crystals precipitating on cooling are filtered off and washed with ethanol. After drying, 2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-(2,3-dihydroxypropyl)acetamide remains as colorless crystals of m.p. 180-181 °C.

Example 27: 2-[3,5-Bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-(2-morpholin-4-yl-ethyl)-acetamide

5.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetate (Example 2) and 2.9 ml of 4-(2-aminoethyl)morpholine are boiled under reflux for 18 h in 50 ml of tetrahydrofuran. The mixture is cooled, poured onto water and extracted with ethyl acetate. The combined organic phases are dried over sodium sulfate and concentrated on a rotary evaporator. The residue is crystallized

from isopropanol. After drying, 2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-(2-morpholin-4-yl-ethyl)acetamide remains as colorless crystals of m.p. 180-182 °C.

Example 28: 2-[3,5-Bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-(2-hydroxyethyl)-N-methyl-acetamide

2.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetate (Example 2) and 8 ml of N-methylethanolamine are heated at 60 °C for 1 h. The mixture is cooled, poured onto water and extracted with ethyl acetate. The combined organic phases are dried over sodium sulfate and concentrated on a rotary evaporator. The residue is crystallized from isopropanol. After drying, 2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-(2-hydroxy-ethyl)-N-methylacetamide remains as colorless crystals of m.p. 101-104 °C.

Example 29: 2-[3,5-Bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-[2-(2-hydroxyethoxy)ethyl]-acetamide

2.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetate (Example 2) and 10 ml of 2-(2-aminoethoxy)ethanol are stirred at room temperature for 2 h. The mixture is poured onto water and extracted with ethyl acetate. The combined organic phases are dried over sodium sulfate and concentrated on a rotary evaporator. The residue is crystallized from isopropanol. After drying, 2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-[2-(2-hydroxy-ethoxy)ethyl]acetamide remains as colorless crystals of m.p. 173-174 °C.

Example 30: N-{2-[Bis(2-hydroxyethyl)amino]ethyl}-2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetamide

2.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetate (Example 2) and 1.0 g of N,N-bis(2-hydroxyethyl)ethylenediamine are boiled under reflux for 24 h in 8 ml of ethanol. The mixture is cooled, poured onto water and extracted with ethyl acetate. The combined organic phases are dried over sodium sulfate and concentrated on a rotary evaporator. The residue is chromatographed on silica gel. After concentration and drying, N-{2-[bis(2-

hydroxyethyl)amino]ethyl]-2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetamide remains as a colorless foam. R_f value: 0.35 (silica gel 60, methylene chloride/methanol = 9/1). $^1\text{H-NMR}$ (DMSO-d_6): 2.5 (m, 6H), 3.1 (m, 2H), 3.4 (m, 4H), 4.2 (bs, 2H), 4.9 (s, 2H), 7.0 (m, 4H), 7.4 (m, 3H), 7.95 (d, 1H), 8.1 (t, 1H), 11.0 ppm (s, 1H).

Example 31: 2-[3,5-Bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-(2-hydroxy-1-hydroxymethyl-ethyl)acetamide

2.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetate (Example 2) and 2.0 g of 2-amino-1,3-propanediol are boiled under reflux for 3 h in 8 ml of ethanol. The crystals precipitating on cooling are recrystallized from isopropanol. After drying, 2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-(2-hydroxy-1-hydroxymethylethyl)acetamide remains as colorless less crystals of m.p. 212-214 °C.

Example 32: 2-[3,5-Bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-[2-(4-methylpiperazin-1-yl)-ethyl]acetamide

3 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetate (Example 2) and 2.5 g of 2-(4-methylpiperazin-1-yl)ethylamine are boiled under reflux for 20 h in 40 ml of ethanol. The mixture is cooled, poured onto water and extracted with ethyl acetate. The combined organic phases are dried over sodium sulfate and concentrated on a rotary evaporator. The residue is chromatographed on silica gel. After concentration and drying, 2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N-[2-(4-methylpiperazin-1-yl)ethyl]acetamide is obtained as a colorless foam. R_f value: 0.17 (silica gel 60, methylene chloride/methanol = 9/1). $^1\text{H-NMR}$ (DMSO-d_6): 2.1 (s, 3H), 2.3 (m, 10H), 3.15 (m, 2H), 4.9 (s, 2H), 7.0 (m, 4H), 7.4 (m, 3H), 8.0 (m, 2H), 11.0 ppm (s, 1H).

Example 33: 2-[3,5-Bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N,N-dimethylacetamide

2.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]acetate (Example 2) are dissolved in 15 ml of ethanolic dimethylamine (33 per cent) and the solution is stirred at 60°C for 20 h. The crystals precipitating on cooling are recrystallized from isopropanol. After drying, 2-[3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol-1-yl]-N,N-dimethylacetamide remains as colorless crystals of m.p.

DECLARATION AND POWER OF ATTORNEY FOR U.S. PATENT APPLICATIONS

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,
and

I believe I am an original, first and joint inventor of the subject matter which is claimed
and for which a patent is sought on the invention entitled

SUBSTITUTED 3,5-DIPHENYL-1,2,4-TRIAZOLES AND THEIR
USE AS PHARMACEUTICAL METAL CHELATORS

the specification of which is attached hereto.

I hereby state that I have reviewed and understand the contents of the above identified
specification, including the claims.

I acknowledge my duty to disclose all information which is known by me to be material to
the patentability of this application as defined in 37 C.F.R. §1.56.

I hereby claim the benefit under 35 U.S.C. §119(a)-(d) or §365(b) of any foreign
application(s) for patent or inventor's certificate listed below and under 35 U.S.C. §365(a) of any
PCT international application(s) designating at least one country other than the United States
listed below and have also listed below any foreign application(s) for patent or inventor's
certificate or any PCT international application(s) designating at least one country other than the
United States for the same subject matter and having a filing date before that of the application
the priority of which is claimed for that subject matter:

<u>Country, Region or PCT</u>	<u>Application No.</u>	<u>Filing Date</u>	<u>Priority Claimed</u>
Switzerland	1593/96	June 25, 1996	Yes

I hereby claim the benefit under 35 USC §119(e) of any United States provisional
application(s) listed below:

None

I hereby claim the benefit under 35 U.S.C. §120 of any United States application(s) listed below and under 35 U.S.C. §365(c) of any PCT international application(s) designating the United States listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in said prior application(s) in the manner required by the first paragraph of 35 U.S.C. §112, I acknowledge the duty to disclose all information known by me to be material to patentability as defined in 37 C.F.R. §1.56 which became available between the filing date(s) of the prior application(s) and the national or PCT international filing date of this application:

<u>United States Application No.</u>	<u>United States Filing or §371 Date</u>	<u>Status or U.S. Patent No.</u>	<u>International Application No.</u>	<u>International Filing Date</u>
09/202,769	December 21, 1998	Pending	PCT/EP97/03315	June 24, 1997

I hereby appoint the attorneys and agents associated with Customer No. 001095, respectively and individually, as my attorneys and agents, with full power of substitution and revocation, to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith.

I hereby authorize my aforementioned attorneys and agents and any others acting on my behalf to take any action relating to this application based on communications from the Patents and Trademarks Division of Novartis Services AG, Basle, Switzerland, or an affiliate thereof or a successor thereto, without direct communication from me.

Please address all communications to the address associated with Customer No. 001095, which is currently Thomas Hoxie, Novartis Corporation, Patent and Trademark Dept., 564 Morris Avenue, Summit, NJ 07901-1027.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

FIRST JOINT INVENTOR:

Full name : **Rene Lattmann**

Signature : _____

Date : _____
(MM/DD/YY)

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Switzerland

SECOND JOINT INVENTOR:

Full name : **Pierre Acklin**

Signature : _____

Date : _____
(MM/DD/YY)

Citizenship : Switzerland

Residence : Basel, Switzerland

P.O. Address : Markgraeflerstr. 47
4057 Basel
Switzerland

IMPORTANT: Before this declaration is signed, the patent application (the specification, the claims and this declaration) must be read and understood by each person signing it, and no changes may be made in the application after this declaration has been signed.

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,465,504 B1
DATED : October 15, 2002
INVENTOR(S) : Rene Lattmann et al.

Page 1 of 2

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title page,

Item [75], should read

-- [75] Inventors: **René Lattmann**, Binningen; **Pierre Acklin**, Basel, both of (CH) --.

Item [30], should read

-- [30] **Foreign Application Priority Data**

Jun. 25, 1996 (CH) 1593/96 --.

Column 7,

Line 63, should read -- alkyl, halo-lower alkyl, lower alkoxy or nitrile; R₆ and --.

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Column 17,

Line 17, should read -- dimethylaminobenzyl)-IH-[1,2,4]triazole remains as colorless --.

Line 58, should read -- remains as colorless crystals of m.p. 268-269° C. --.

Column 18,

Line 24, should read -- 2.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol- --.

Column 19,

Line 34, should read -- ethoxy)ethyl]acetamide remains as colorless crystals of m.p. --.

Line 42, should read -- yl]acetate (Example2) and 1.0 g of
N,N-bis(2-hydroxyethyl) --.

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,465,504 B1
DATED : October 15, 2002
INVENTOR(S) : Rene Lattmann et al.

Page 2 of 2

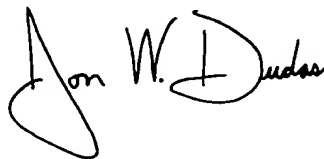
It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 19 (cont'd).

Line 53, should read -- 2H), 4.9 (s, 2H), 7.0 (m, 4H), 7.4 (m, 3H), 7.95 (d, 1H), 8.1 (t, 1H), 11.0 --.

Signed and Sealed this

Seventh Day of March, 2006

A handwritten signature in black ink, appearing to read "Jon W. Dudas". The signature is stylized with a large, looped initial "J" and a distinct "D" for "Dudas".

JON W. DUDAS
Director of the United States Patent and Trademark Office

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO : 6,465,504 B1
DATED: : OCTOBER 15, 2002
INVENTOR(S) : RENE LATTMANN ET AL

Ping 1993

It is certified that there are errors in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title page

Item (75) should read:

-- (75) Inventors: **René Lattmann**, Binningen; **Pierre Acklin**, Basel, both of (CH) --.

Item (30) should read:

-- (30) **Foreign Application Priority Data**

Jun. 25, 1996 (CH)1593/96 --.

Column 7

Line 63 should read:

-- alkyl, halo-lower alkyl, lower alkoxy or nitrile; R₆ and --.

✓

Column 8

Line 10 should read:

-- formula II in which --.

11

MAILING ADDRESS OF SENDER:

Joseph J. Borovian

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(862) 778-7801

PATENT NO. 6,465,504 B1

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO : 6,465,504 B1
DATED: : OCTOBER 15, 2002
INVENTOR(S) : RENE LATTMANN ET AL

It is certified that there are errors in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 16

Last line should read:

-- [1,3]oxazin-4-one are boiled under reflux for 5 h with 1.7 g --.

Column 17

Line 17 should read:

-- dimethylaminobenzyl)-IH-[1,2,4]triazole remains as colorless --.

Line 58 should read:

-- remains as colorless crystals of m.p. 268-269° C. --.

Column 18

Line 24 should read:

--2.0 g of ethyl [3,5-bis(2-hydroxyphenyl)-[1,2,4]triazol- --.

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